Diaries in Clinical Trials: When and How?

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Objectives

1. Why should you consider the use of diaries for a clinical trial?
2. How does one think about planning and implementing a diary study?
3. An example of an clinical trial using diaries as one of the primary outcome measures.

1.
Why should you consider diaries in a clinical trial?

You won't be the first: 25% of all FDA trials employ diaries

Several companies provide diary data collection services

Why should you consider diaries in a clinical trial?

A. Because you need a fine-grained resolution of the phenomena or associations than is possible with typical measures.

1. Time to pain/sx relief due to a treatment
2. Diurnal rhythms of activities, affect, symptoms
3. Duration of treatment effects
4. Effects of social interactions on outcomes
5. Minor stressors impact on physiological variables
6. Precursors of substance use
7. Sleep quality's association with immune variables
8. Medication compliance role in outcomes
9. Changes in activities of daily living and other health behaviors

Why should you consider diaries in a clinical trial?

B. Because some or all of your variables are subject to retrospective recall bias that might bias the measurement (Ecological Validity)

Patient Reported Outcomes (PROs)

- Many assessments are based on self-reports
  - Subjective states
    - Mood
    - Depression
    - Fatigue
    - Pain
    - Quality of Life
  - Self observations
    - Symptoms
    - Behaviors
      - Health behaviors
      - Treatment compliance
      - Sexual activities
      - Consumption
- Reports not based on Self-report
  - *Some* Interview data, but much is self-report based
  - Physiological measure
  - Archival records
  - Behavioral observations
  - Mortality

Patient Reported Outcomes (PROs)

How are they answered?

- Yes/No
- 5-, 7-, 10-point scales
  - Each point anchored
  - End-points anchored
- Visual Analog Scales (VAS)
- Lists of alternatives
- Frequency
  - "How many …."
- Dating of events
  - "When did…"
- Narrative
  - Later coding difficult

Compared to what?

- Physiological tests
  - BP; EKG; White cell count; fever; lung function
- Direct observations
  - Size/type of lesion; functional ability; death
- Physician/Observer judgments
  - Disease activity ratings

What do we know about memory that is relevant to these questions?

- Selectivity
  - Encoding is selective
  - Decoding is selective
- Capacity Limitations
  - Nonsense syllables
- Memory Distortion
  - Perceptions of football game
  - Recovered memories
  - Remembrance of Life Events

Experiential to Semantic Memory Shift

Psychological Bulletin
2002, Vol. 128, No. 6, 934–960

0033-2909/02/$5.00 DOI: 10.1037//0033-2909.128.6.934

Belief and Feeling: Evidence for an Accessibility Model of Emotional Self-Report

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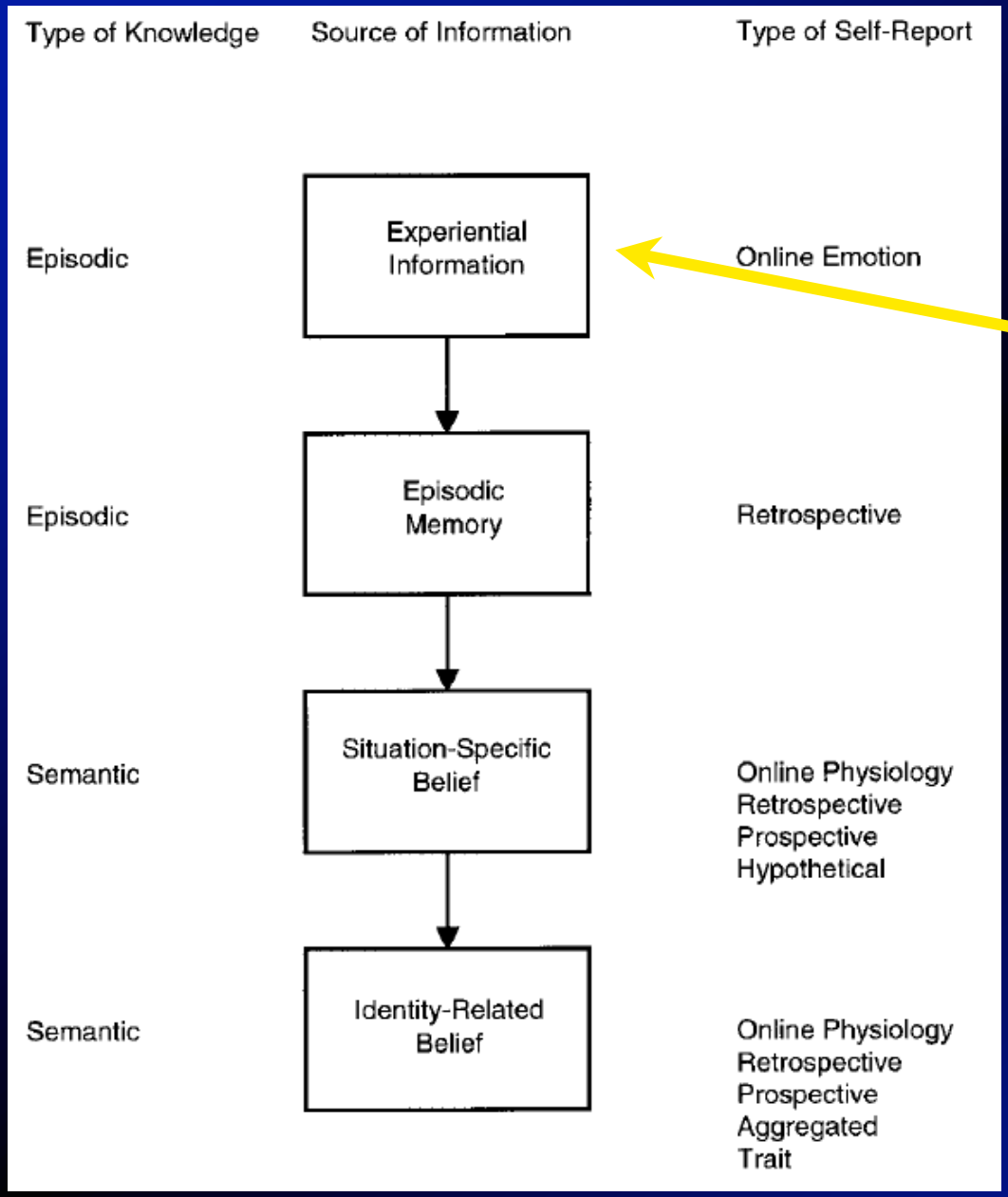
This review organizes a variety of phenomena related to emotional self-report. In doing so, the authors offer an accessibility model that specifies the types of factors that contribute to emotional self-reports under different reporting conditions. One important distinction is between emotion, which is episodic, experiential, and contextual, and beliefs about emotion, which are semantic, conceptual, and decontextualized. This distinction is important in understanding the discrepancies that often occur when people are asked to report on feelings they are currently experiencing versus those that they are not currently experiencing. The accessibility model provides an organizing framework for understanding self-reports of emotion and suggests some new directions for research.

Experiential to Semantic Memory Shift

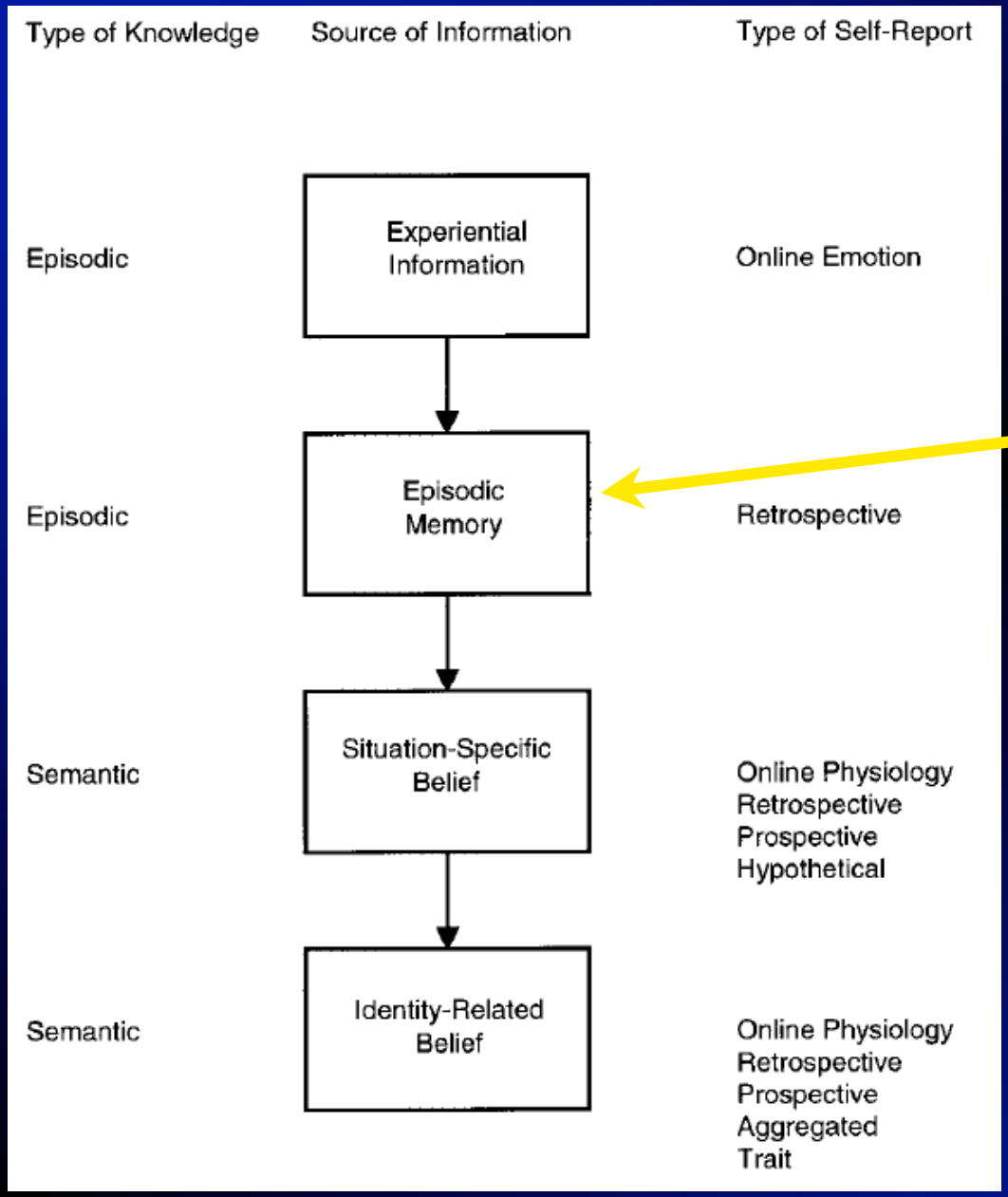
We offer an accessibility model of emotional self-report as an organizational framework. The model is based on standard cognitive principles of accessibility and priming. According to this model, when data from current experience is inaccessible, self-reports of emotion will reflect other sources of nonexperiential information. These other sources of information include memory for the episodic details of an emotional event as well as semantic knowledge about one's emotions. Our review of relevant studies

Experiential to Semantic Memory Shift



- Immediate experience about an emotion or symptom. Information is available with thought.

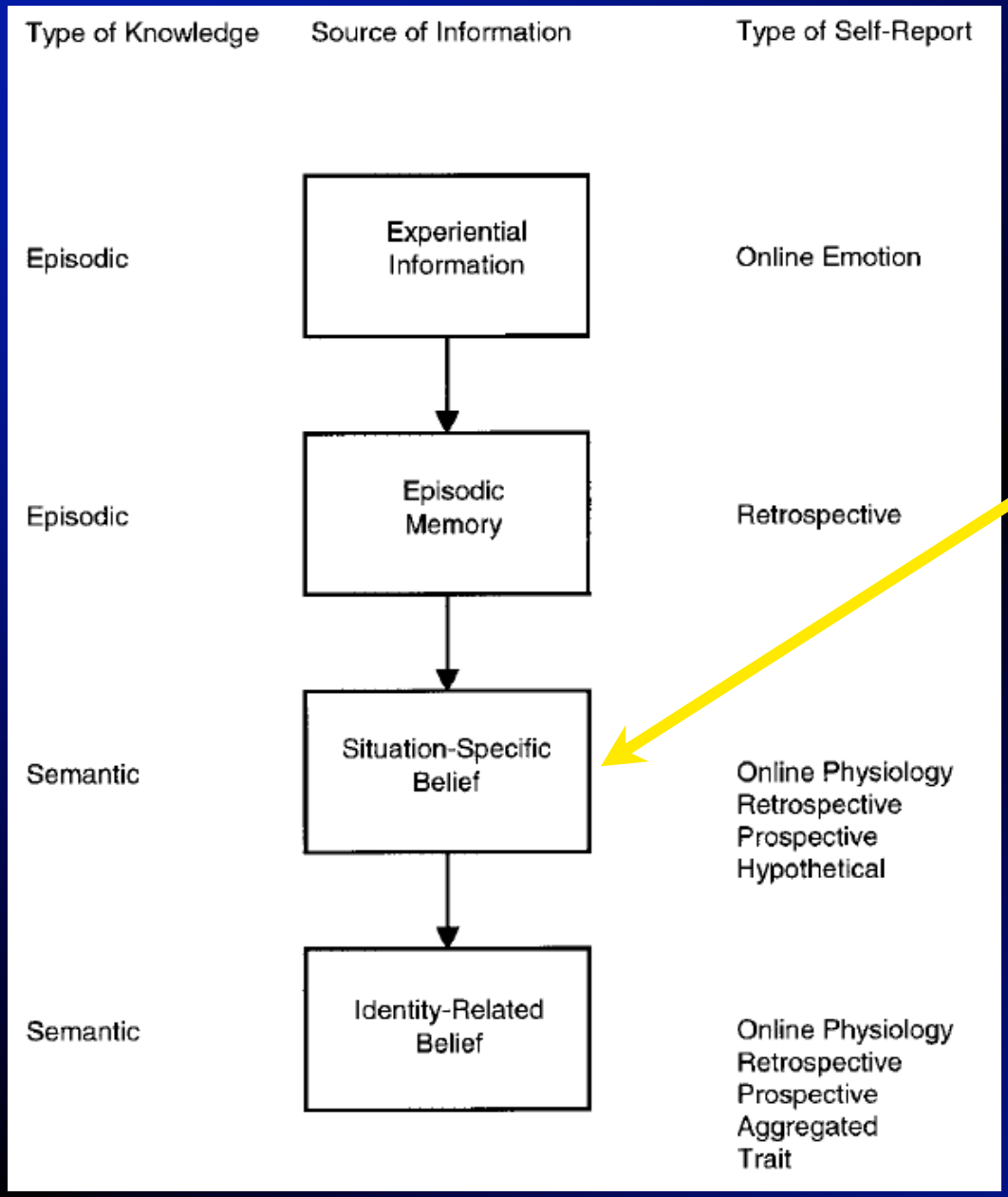
Why should you consider diagries in a clinical trial?



Experiential to Semantic Memory Shift

- Information not available, but a recent instance is. Example: remembering the feeling of being on a rollercoaster.

Why should you consider diagries in a clinical trial?



Experiential to Semantic Memory Shift

- Information not available. However, you have knowledge of the usual experience. Birthdays are usually pleasant.

Their Argument

- Emotions experiences can not be retrieved
  - "Reenacted" emotions differ from original
  - Person never feels the same thing twice
- Distinction between Real-time and Memory-based assessments
- Retrospective and hypothetical reports are biased by similar things, e.g., gender
- Recalling the context of an event can help a person reconstruct their emotional memory, but context memory declines quickly
- As context memory declines, then people shift to semantic memory
  - This creates a set biases based on semantic memory

Their Argument

- When an even is not strongly associated with situation-specific beliefs, then more general, identity-related beliefs are used
  - Related to personality
  - Related to social norms
    - Belief that love deepens over time vs on-line reports
    - Women are more emotional
- Another example from DRM research
  - Recall of last interaction with child

Immediate Context

- People use context as information and judge the quality and relevance of the information
- Memory for pain, for instance

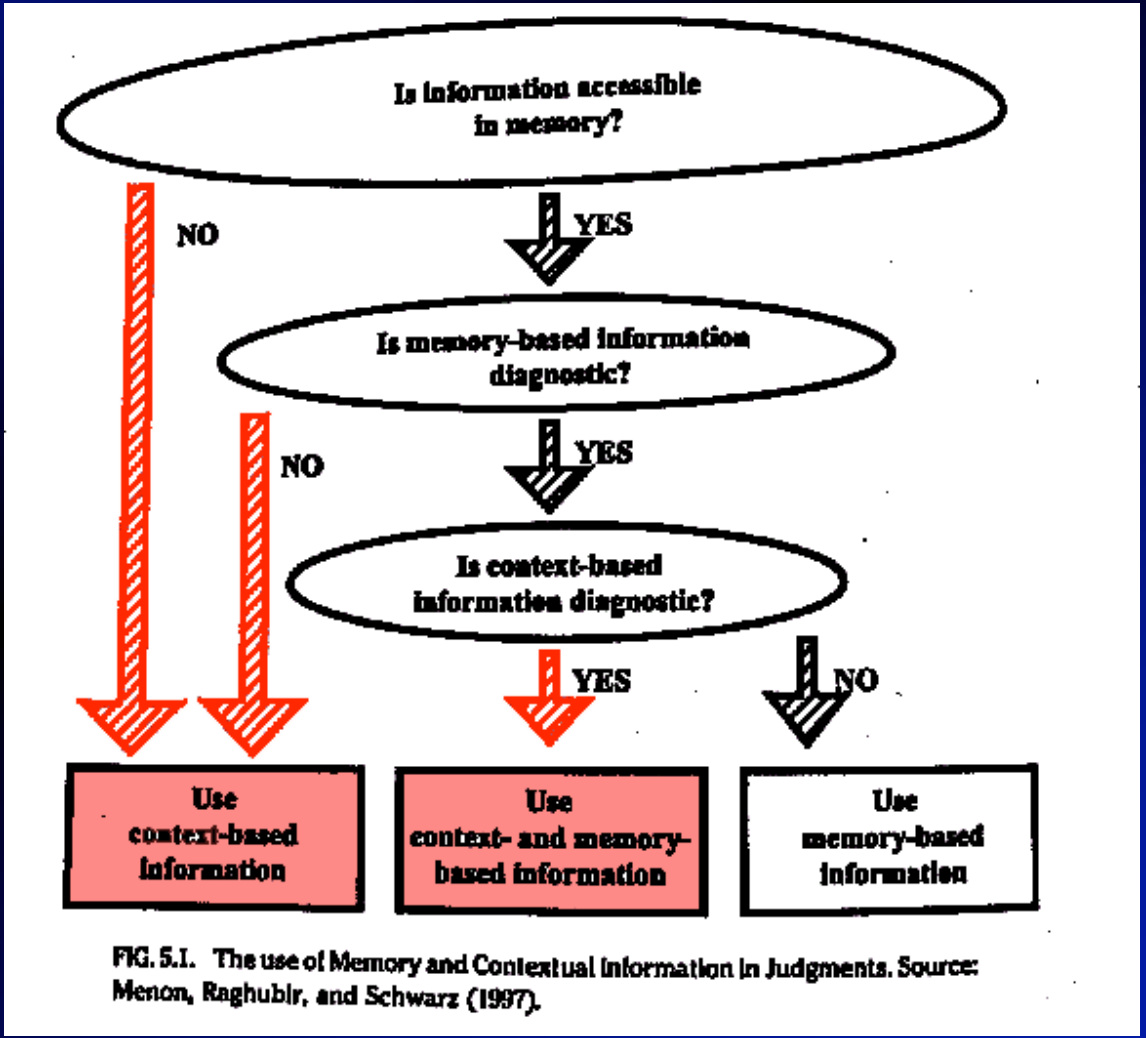
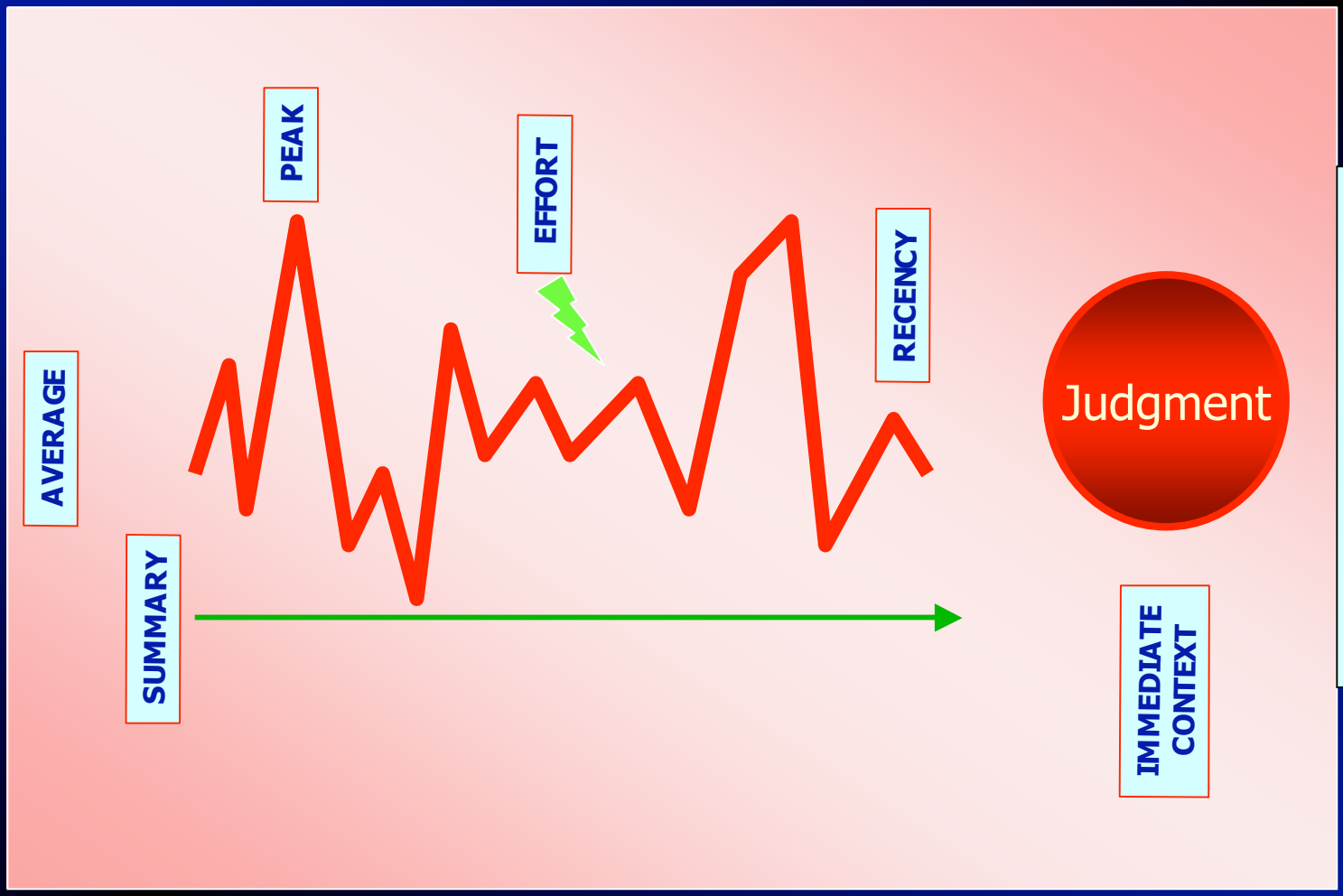


FIG. 5.1. The use of Memory and Contextual Information in Judgments. Source: Menon, Raghubir, and Schwarz (1997).

Schematic of Judgment Process



Person Factors

- Neuroticism
- Depression
- Optimism
- Private Self-Consciousness

- Motivation to dissemble

Peak and Recency

Colonoscopy pain Duration Neglect

- ***Redelmeier, D., & Kahneman, D. (1996). Patients' memories of pain medical treatments: Real-time and retrospective evaluations of two minimally invasive procedures.*** **Pain, 66, *3-8.***
- ***Fredrickson JSPB 2001 review***

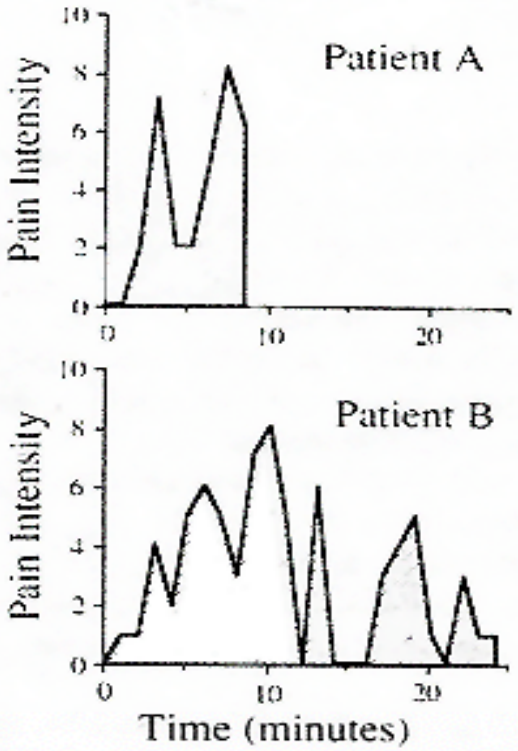
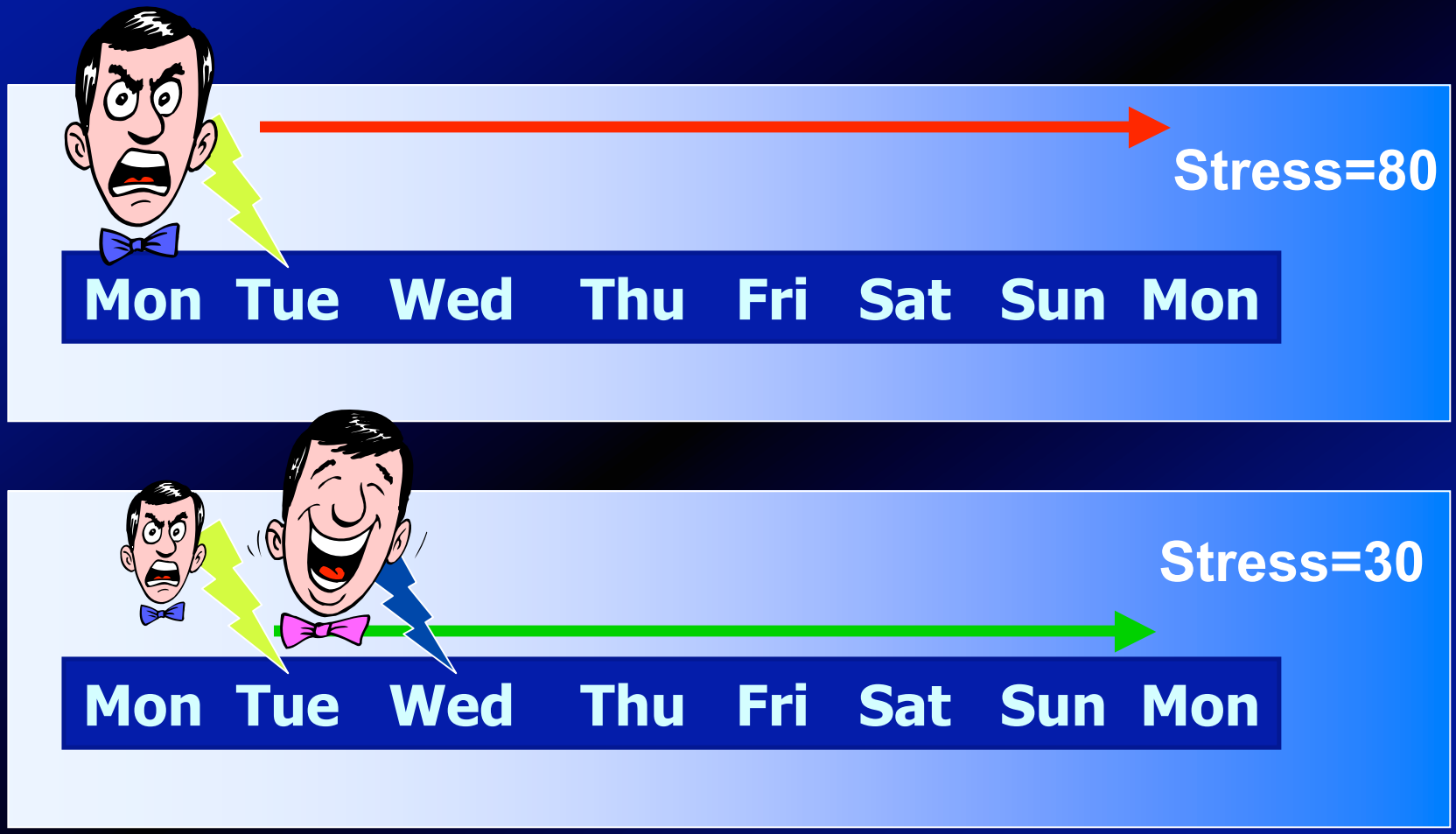


Fig. 1. Real-time recordings from two patients. Each graph displays the intensity of pain recorded each minute by a patient undergoing colonoscopy. The experiences of two individuals are shown (Patient A and Patient B). The *x*-axis represents time in minutes from the start of the procedure. The *y*-axis represents the intensity of pain recorded in real-time on a visual analogue scale with ends denoted as 'no pain' and 'extreme pain'. The procedure lasted 8 min for Patient A and 24 min for Patient B.

Effort-after-meaning



Summary Processes

What, exactly, do we mean when we ask *"How was X over the last week?*

- **About the average of all moments?**
- **We're not explicit with participants**
- **People over-emphasize:**
  - **salient events**
  - **intense experiences**
  - **recent occurrences**
  - **mood congruent events**

Immediate Context

Questionnaire #1

1. Taking all things in consideration, how satisfied are you with your life these days?

2. How is satisfied are with your spouse/significant other relationship?

R = .11

Questionnaire #2

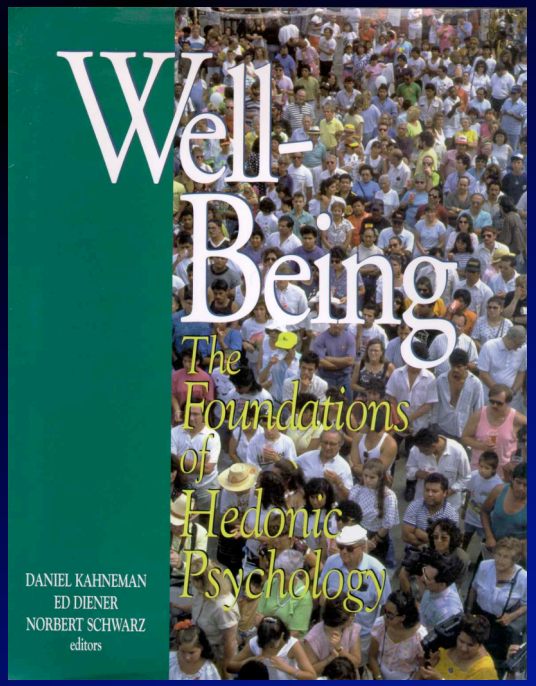
1. How satisfied are with your spouse/significant other relationship?

2. Taking all things in consideration, how satisfied are you with your life these days?

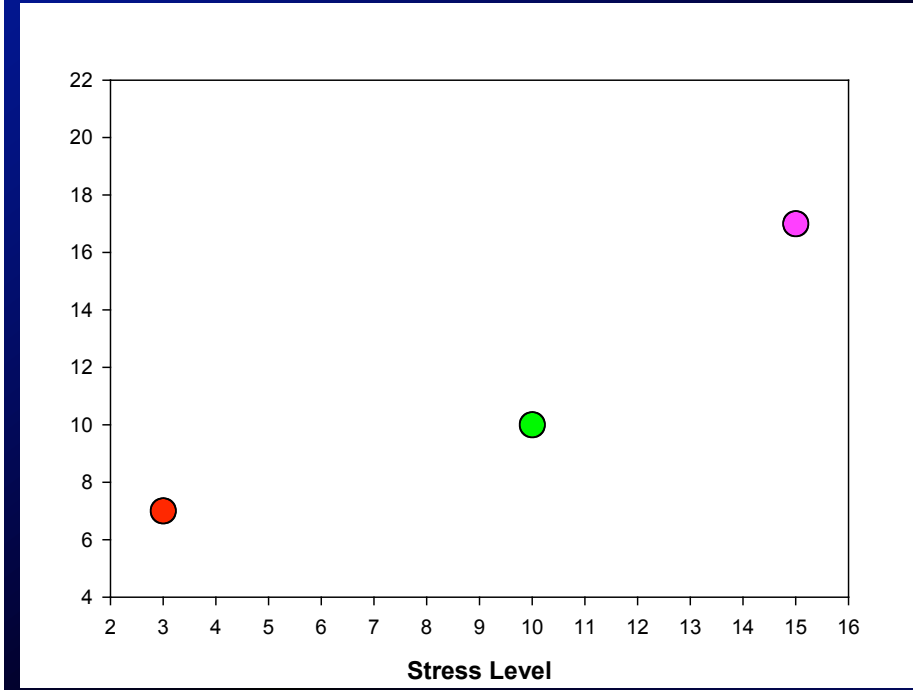
R = .66

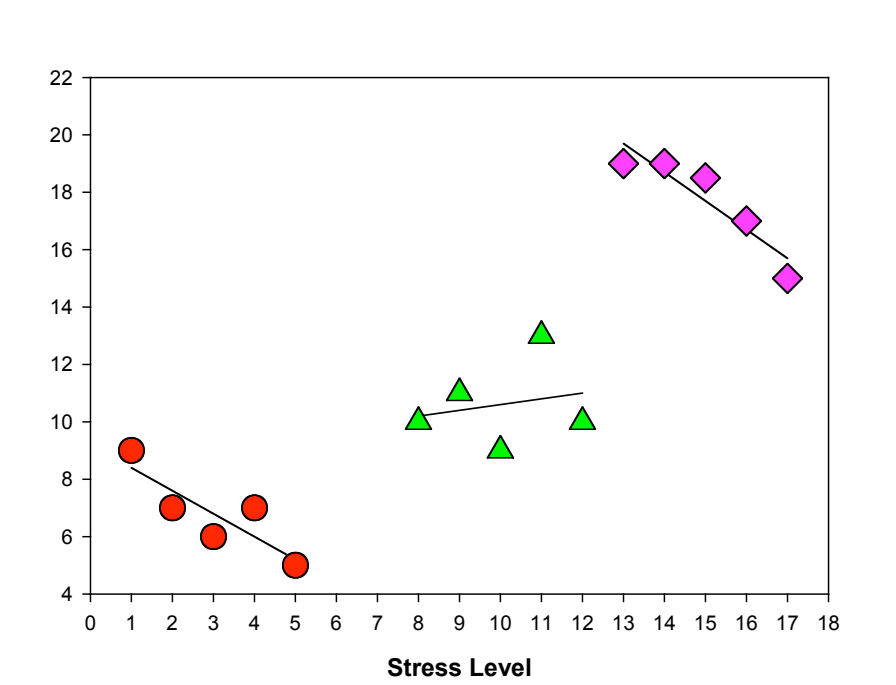
Immediate Context

- **Finding a dime➔ altered SWB**
- **Letterhead of mailed questionnaire**
- **Response options for questions**
- **N. Schwarz, *American Psychologist***



C. Because you are interested in within-person associations





2.

How does one think about planning and implementing a diary study?

Ecological Momentary Assessment

EMA assesses phenomena at the moment they occur

EMA is dependent upon careful timing of assessments

EMA methods usually, but not always, involve a substantial number of repeated observations

EMA measurements are made in the environments that subjects typically inhabit

Modality of data collection

- Sampling
  - End-of-day
  - Throughout-the-day
- Paper-and-pencil
  - Common
    - Compliance
    - Readability
- Electronic diary
  - Palmtop computers
  - Time-date stamp
  - Branching
- Signaling devices
  - Ambulatory monitors
  - Pagers
  - Watches
  - Electronic diaries
- Alternatives
  - IVR
  - Web-based
  - Audio-monitoring

Content

- Situational characteristics
  - Where are you?
  - What are you doing?
  - Who are you with?
- Affective state
  - Mood assessment
  - Depression, anxiety, fatigue
- Targeted content
  - Symptoms
  - Behaviors
  - Subjective states
  - Physiological variables
  - Cognitive performance
- Often standardized from one study to the next

Practicalities

- How often?
  - 1 to 60 times per day
  - 1 to 100s of days
- How many questions?
  - 1 to 30
  - But branching possible with electronic diaries & IVR
- What sorts of schedules?
  - Random
  - Event-driven
  - Combined
- Can people do it?
  - YES
  - All kinds
- How do they feel about doing it?
  - Fine, most of the time
- Does doing it affect their answers (reactivity)?
  - Probably not
- Are there problems?
  - Some

Recording Paradigms

Interval-contingent

Regular, time-based sampling scheme

Examples:
- *Ambulatory blood pressure monitors (15m/30m)*
- *Pain diaries (at the top of the hour)*

Anticipation of signals
Environment entrained to clock
Simple to implement

Event-contingent

Sample of basis of event occurrence

Examples:
- *Record just before smoking*
- *Immediately after a meal*
- *When feeling stressed*

Based on participant's ability to recall prompting instructions
False negatives very likely
Not representative of experience
Efficient for certain questions

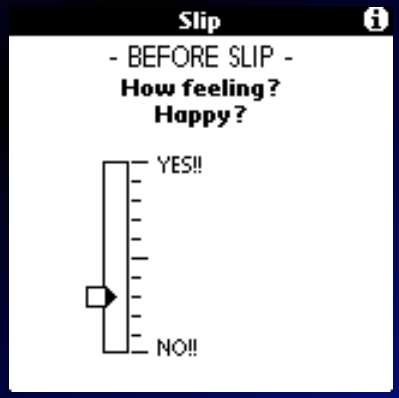
Signal-contingent

Sample when signaled

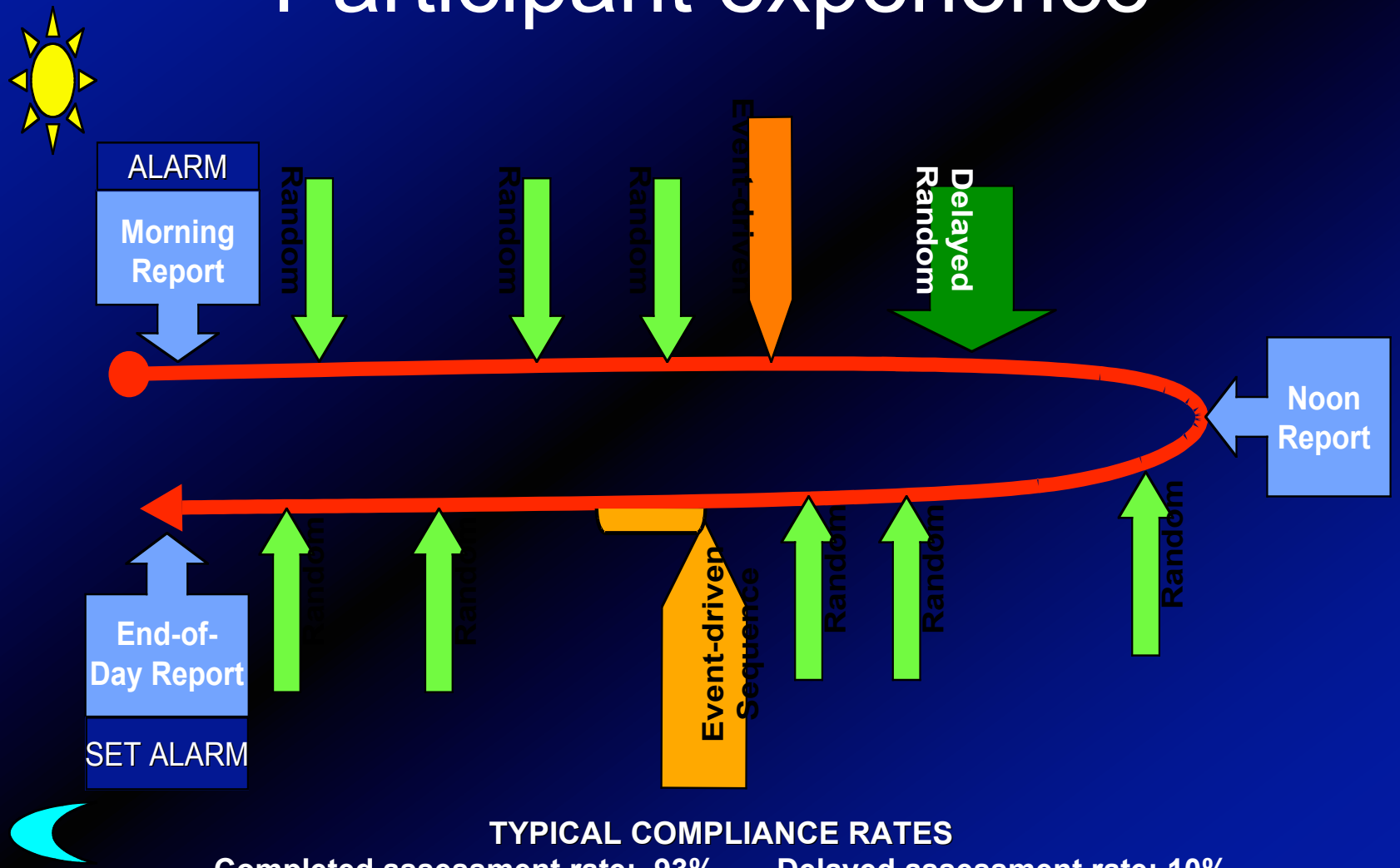
Examples:
- *ESM, random*
- *EMA, random*
- *Different types of random schedules: pure, stratified within intervals*

Most representative of experience
May miss critical events
Complexities of implementation

Electronic Diary Screens



Participant experience



TYPICAL COMPLIANCE RATES

Completed assessment rate: 93% Delayed assessment rate: 10%

Suspensions Activated: <1 Suspensions deactivate rate: 60% Suspension (min): 25

Compliance-enhanced Electronic Diary

Auditory signal prior to targeted times

Actual feedback about compliance

User-friendly

Actual Compliance: 94%

3.
An example of a clinical trial using diaries as one of the primary outcomes

An example with diaries as a of the primary outcomes

- Purpose:
  - Pharmaceutical company wanted to know if their new compound was effective in treating symptoms of fibromyalgia
  - Acceptable for FDA submission: Phase 2
- Design:
  - 2 week baseline period; 2 week dose titration period; 8 week follow-up period
  - Ss randomized to active tx versus placebo
  - Questionnaires taken Pre-baseline, Pre-Titration, Post-Titration, and at 8-week Follow-up
- Outcomes
  - Global Impression of Change
  - Fibromyalgia Impact Questionnaire (FIQ)
  - Within-day diaries
- The Tension
  - GIC says a tx-placebo difference whereas diary data does not

An example with diaries as a of the primary outcomes

"Since the start of the study, my overall status is:"

1. Very much improved;
2. Much improved;
3. Minimally improved;
4. No change;
5. Minimally worse;
6. Much worse;
7. Very much worse

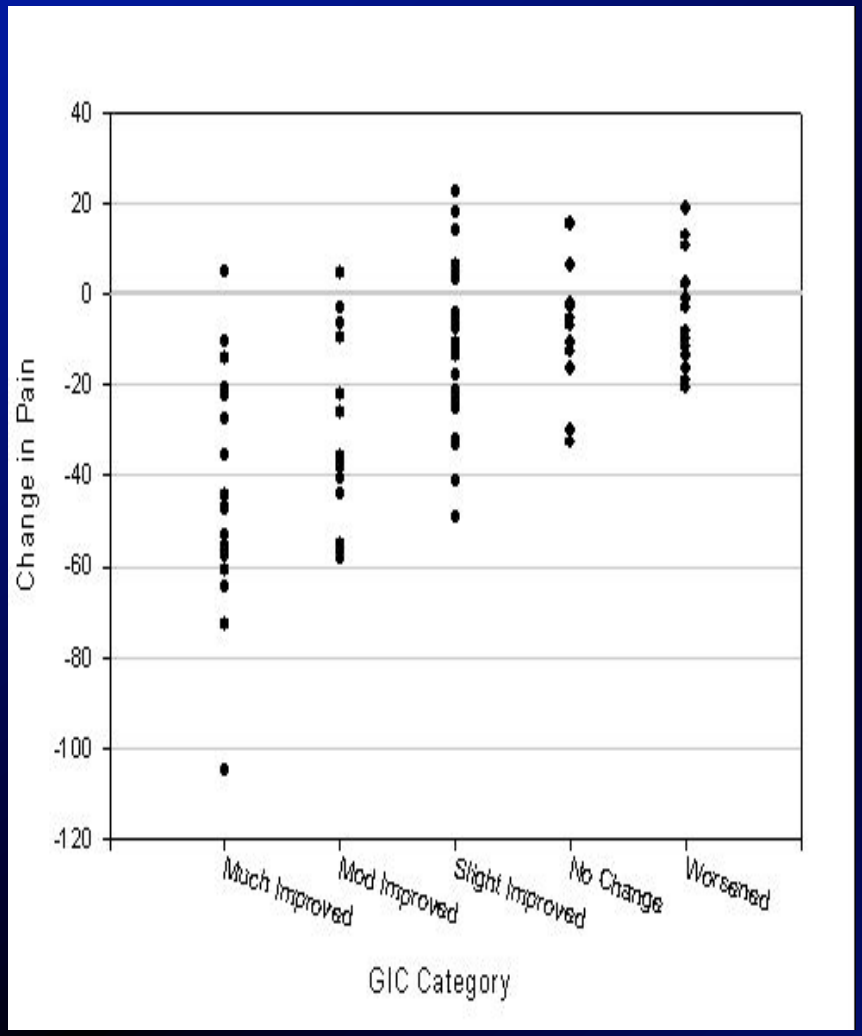
Very much improved,	19 (22%)
Much improved,	14 (16%)
Minimally improved,	24 (28%)
No change,	14 (16%)
Minimally worse,	9 (10%)
Much worse,	5 (6%)
Very much worse,	1 (1%)

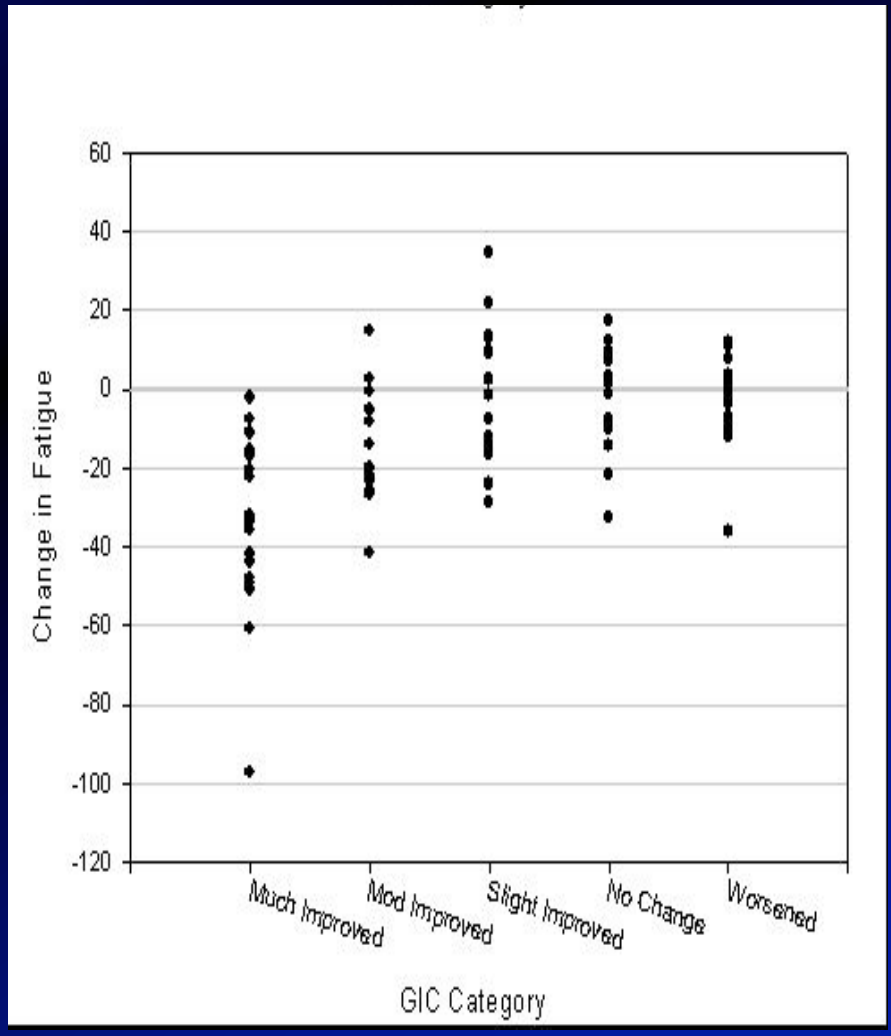
An example with diaries as a of the primary outcomes

[redacted]

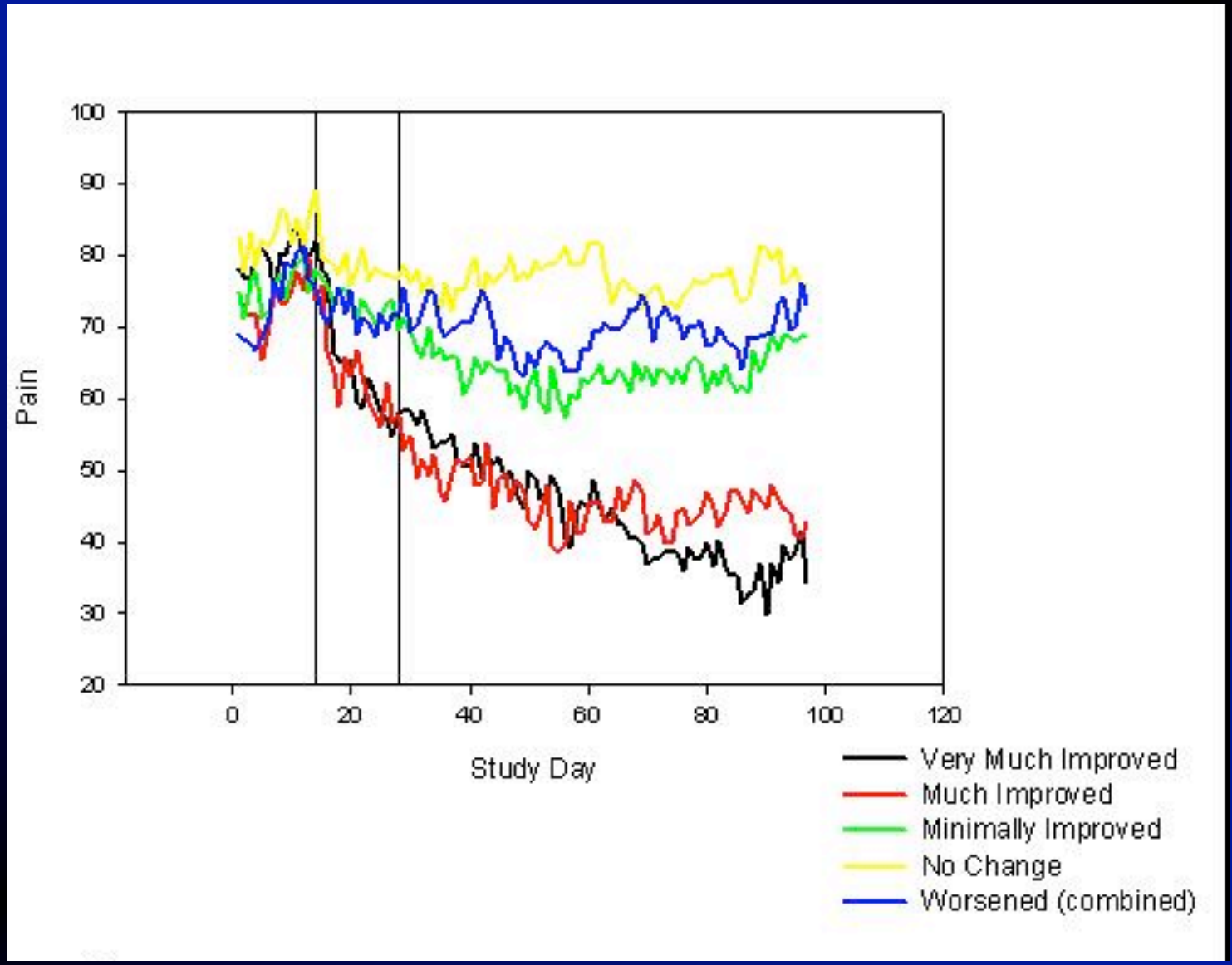
An example with diaries as a of the primary outcomes

The Post minus Pre Change View





An example with diaries as a of the primary outcomes



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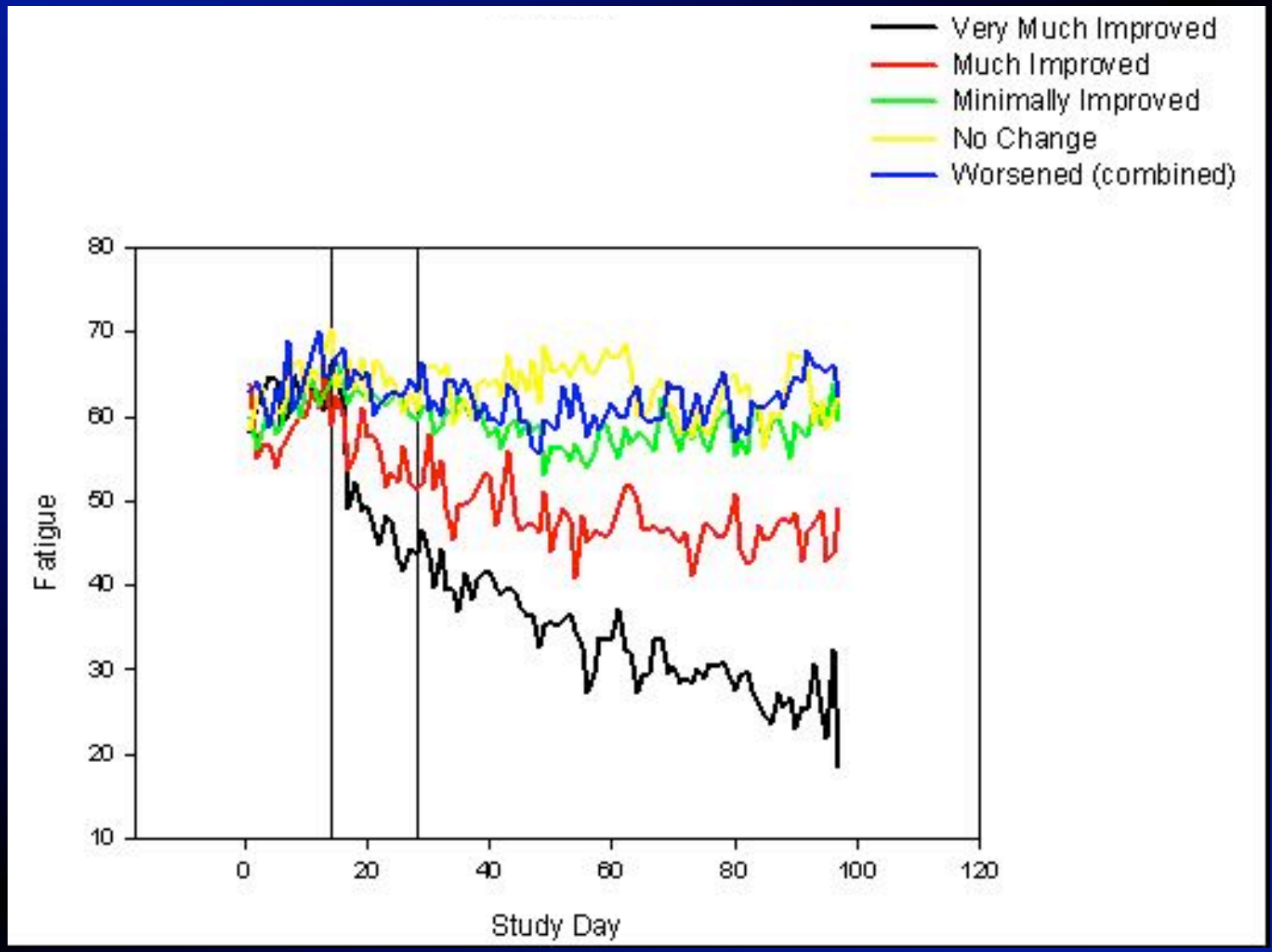
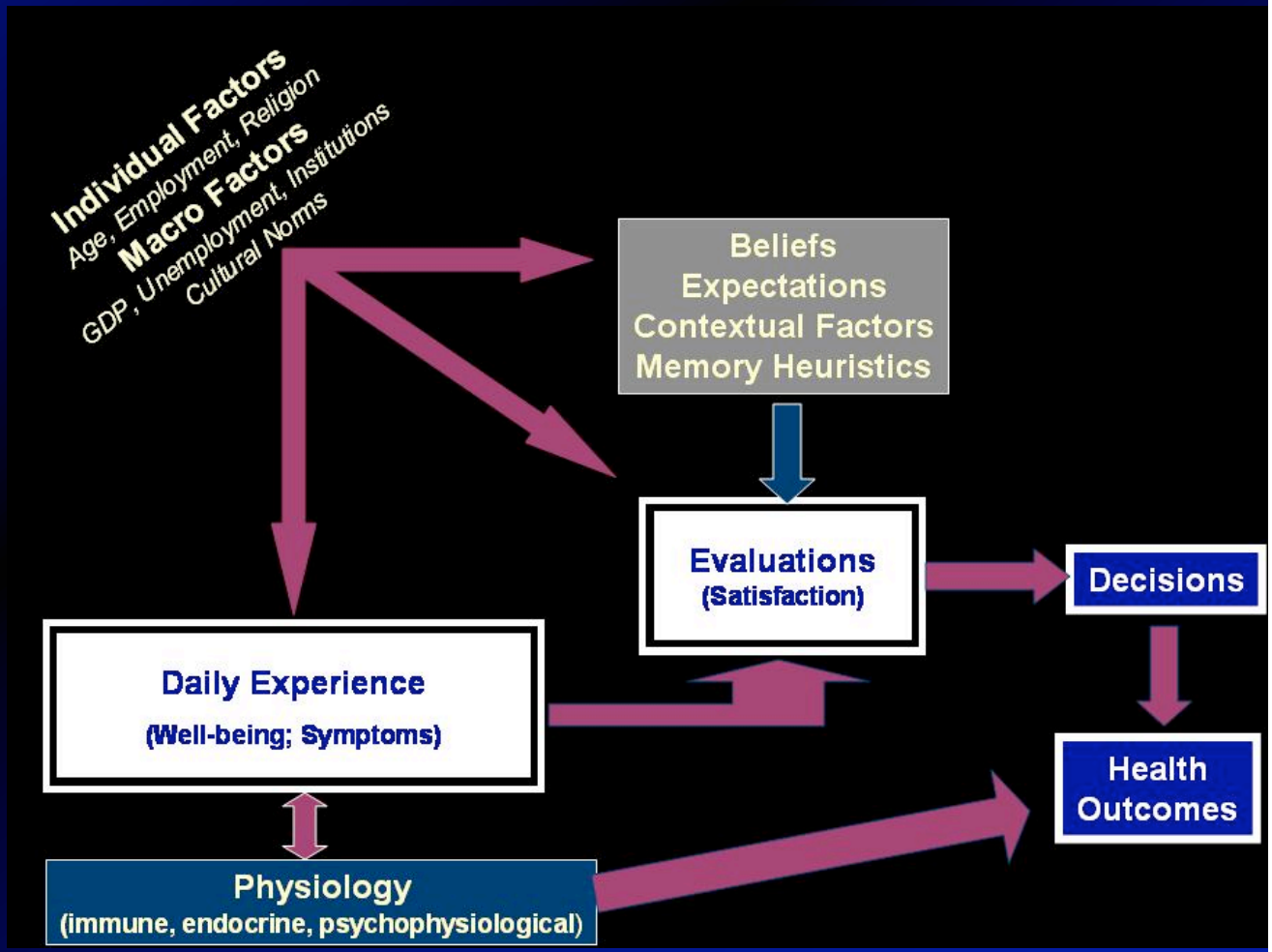


Two Types of Information: Recall and Momentary

- Which is correct?
- Depends on the purpose of the research
  - Colonscopy again?
  - Vacation again?



More Discussion